

Polyuria and Polydipsia  
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Introduction

Polyuria and polydipsia (PU / PD) refer to excessive water consumption and urine production respectively. These are common clinical signs in both dogs and cats. Water consumption exceeding 100 ml/kg or urine production exceeding 50 ml/kg body weight per day is considered abnormal and should be pursued. These numbers have been established in laboratory reared dogs and may not reflect "normal" water consumption in pets. They are to be used only as guidelines. Water consumption can vary greatly from day to day so it is important to have owners subjectively assess water consumption in the home environment for several consecutive days in order to obtain an accurate picture before beginning unnecessary and expensive diagnostic tests. Actual quantification of water consumption can be very difficult and may not be practical for the majority of pet owners.

Normal Water Homeostasis

Extracellular fluid volume is maintained by regulation of fluid intake and urine production. The thirst center is stimulated by an increase in plasma osmolality (sodium concentration) and/or a decrease in blood volume (hypovolemia) resulting in an increase in water consumption. Increasing plasma osmolality and hypovolemia also stimulate osmoreceptors in the anterior hypothalamus and baroreceptors in the aortic arch resulting in the release of antidiuretic hormone (ADH) from the anterior pituitary. ADH circulates and binds to receptors on the renal tubular cells of the distal tubules and collecting ducts resulting in the production of cAMP. This causes the opening of pores in the luminal membrane of the tubular cells and allows for reabsorption of water from the glomerular filtrate resulting in a concentrated urine. In order for water to be pulled out of the tubule it must move along a concentration gradient maintained by the hypertonic renal medullary interstitium. Loss of this gradient (medullary washout), will result in an inability to concentrate urine even in the face of normal ADH activity. Urea and sodium are largely responsible for maintaining the hypertonicity of the interstitium. E. The sensation of thirst and secretion of ADH are suppressed when plasma osmolality and blood volume are returned to normal.

Differential Diagnosis: Mechanisms of PU/PD

A. Renal disease:

1. Chronic renal failure: A decrease in the number of functional nephrons causes an increase in tubular flow in the remaining nephrons and leads to a solute diuresis. A decrease in urine concentrating ability may be the only laboratory abnormality indicating renal disease (especially in feline patients) presented for PU/PD.
2. Pyelonephritis: Bacterial induced tubular destruction and an increase in renal blood flow cause a decrease in medullary hypertonicity.
3. Primary renal glycosuria (Fanconi's Syndrome): A proximal tubular defect results in renal glycosuria leading to an osmotic diuresis. The blood glucose is normal.
4. Post-Obstructive diuresis: May be seen in previously blocked cats. Due to osmotic diuresis from loss of large amounts of sodium and urea into the urine following relief of urethral obstruction.

B. Diabetes mellitus:

Hyperglycemia results in glycosuria and an osmotic diuresis. Threshold for renal glycosuria is a blood glucose of 180 – 220 mg/dl (dog) and 240 – 300 mg/dl (cat).

C. Liver disease:

PU/PD may occur as the result of: (1) decreased production of urea which is a major component of the hypertonic medullary interstitium, (2) increased renin and

cortisol levels due to a lack of hepatic degradation, (3) increased aldosterone concentration leading to increased sodium concentration, and (4) hypokalemia (see hypokalemic nephropathy).

D. Hyperthyroidism:

Increased total renal blood flow reducing the tonicity of the medullary interstitium. Psychogenic polydipsia or primary polydipsia is reported in humans with hyperthyroidism.

E. Hypercalcemia:

(1) Interference with cAMP activation by ADH, (2) damage to ADH receptors, and (3) mineralization of renal tubular cells.

F. Hyperadrenocorticism:

Glucocorticoids interfere with the action of ADH at the renal tubule and decrease ADH secretion by reducing osmoreceptor sensitivity to rising plasma osmolality.

G. Hypoadrenocorticism:

Renal sodium wasting leads to decreased medullary hypertonicity.

H. Pyometra:

(1) E. coli endotoxins interfere with sodium reabsorption and damage ADH receptors and (2) may result in an immune-complex glomerulonephritis.

I. Hypokalemia:

(1) Degeneration of renal tubular cells, (2) decreased medullary hypertonicity, (3) stimulation of thirst, and (4) stimulation of renin release.

J. Polycythemia:

Mechanism unknown; may be related to sluggish blood flow in kidney or hypothalamus.

K. Medications:

Exogenous steroids, diuretics, salt supplementation, primidone, phenobarbital, KBr and vitamin D.

L. Pituitary or central diabetes insipidus (CDI):

Due to inadequate production, storage or release of ADH. May occur as a congenital defect or secondary to trauma, mass lesions, infection or infarction of the pituitary or hypothalamus.

M. Nephrogenic diabetes insipidus (NDI):

Congenital structural or functional defects in ADH receptor. Rare in dogs and cats.

N. Primary polydipsia or psychogenic polydipsia:

Underlying cause unknown (possible CNS lesion); results in increased renal blood flow and a decrease in medullary hypertonicity. Extremely uncommon in dogs and cats and is largely a diagnosis of exclusion.

Diagnostic Approach to PU / PD

A. Document PU/PD actually exists. Recommend assessment of water consumption in the home environment. Hospitalized animals frequently do not drink as much as they would in their natural surroundings.

B. Quick evaluation of urine specific gravity and glucose is cheap, easy, and very helpful

in evaluating animals for possible pathologic PU/PD. If the urine specific gravity of a non-glycosuric sample, obtained from a dog or cat without signs of dehydration, is greater than 1.030 (dog) or 1.035 (cat), the likelihood of pathologic PU/PD is small and further work-up may not be required.

C. Most causes of PU/PD will be identified following a good history, physical examination, and an initial data base consisting of a CBC, chemistry profile, and urinalysis with bacteriologic culture.

D. If a cause has not been discovered after step C, the most likely diagnoses are hyperadrenocorticism (dog only, cats with Cushing's are usually overtly diabetic), central and nephrogenic diabetes insipidus, and primary polydipsia. As hyperadrenocorticism is far more common than either of the other causes, an ACTH stimulation test, urine cortisol/creatinine ratio or low-dose dexamethasone suppression test should be performed before proceeding to the modified water deprivation test (See Canine Hyperadrenocorticism).

#### Modified Water Deprivation Test (MWDT)

A. This test is designed to help differentiate CDI, NDI, and primary polydipsia. It is not very helpful unless other causes of PU/PD have been ruled out.

B. The test is designed to determine whether ADH is released in response to dehydration and whether the kidneys can respond to the circulating ADH.

C. **VERY IMPORTANT !! THE TEST SHOULD NEVER BE PERFORMED ON AN ANIMAL WITH PRE-EXISTING AZOTEMIA OR OBVIOUS DEHYDRATION. DOING SO IN ANIMALS WITH RENAL INSUFFICIENCY MAY RESULT IN DECOMPENSATION AND THE DEVELOPMENT OF OLIGURIC RENAL FAILURE OR ANURIC RENAL FAILURE.**

D. Severe dehydration can occur very rapidly (4-6 hours) especially in animals with diabetes insipidus. Leaving them unattended without water for several hours or overnight may result in severe hyperosmolality, coma, and death.

E. Gradual water restriction should be instituted at home for 2-3 days prior to performing the MWDT in order to help minimize medullary washout from long-standing PU/PD.

#### PHASE ONE

1. Animal is weighed, bladder emptied and urine saved for specific gravity and osmolality (if available).
2. Blood is obtained for BUN and osmolality.
3. Water is withheld. BUN, plasma osmolality and body weight are obtained hourly. The bladder is emptied every hour and a sample is saved for specific gravity and osmolality.
4. Test concluded with either a 5% loss in body weight, azotemia (BUN > 30), or urine specific gravity > 1.030 (1.035 cats). The bladder is emptied and urine is saved for specific gravity and osmolality, and plasma is obtained for osmolality.

#### PHASE TWO

1. Aqueous vasopressin (Pitressin) 2 - 3 units (dog) or 0.25 U/# (cat) is given SQ. Alternatively DDAVP may administered into the conjunctival sac (1 - 2 drops for dogs and 1 drop for cats).
2. Urine and plasma osmolality and urine specific gravity are obtained every 30 min for 90 minutes.
3. Bladder must be emptied at every 30 minute sampling period.
4. Water is withheld throughout the test.

#### Interpretation of the MWDT

A. Normal Animals: Following water deprivation will concentrate urine to > 1.030 (dog) or 1.035 (cat). Urine osmolality in excess of 1,200 mOsm/kg.

B. CDI: Unable to concentrate urine in excess of 1.008 (< 300 mOsm/kg). After ADH administration, urine specific gravity should increase to greater than 1.012

with a 50 - 500 % increase in urine osmolality.

C. NDI: Similar to CDI following water deprivation. No further response following ADH injection.

D. Partial CDI: Results depend on how much ADH is available. Following water deprivation urine specific gravity between 1.008-1.019 and urine osmolality between 300 to 1,000 mOsm/kg. Urine specific gravity and osmolality increase after ADH administration. Similar response seen with hyperadrenocorticism and a number of the other causes of PU/PD. This is why it is important to rule-out these processes prior to a MWDT.

E. Primary polydipsia: Depends on degree of medullary washout. With minimal washout results are similar to normal animals. More severe washout gives results similar to partial diabetes insipidus.

#### Treatment of Polyuria and Polydipsia

A. Treat the underlying disorder !

B. Treatment of CDI

1. DDAVP (Desmopressin acetate) 1-2 drops into the conjunctival sac or 0.01 to 0.05 mls subcutaneously SID or BID. May also dose orally with 0.1 to 0.2 mg once or twice a day.

- a. 1 drop = 1.5 to 4.0 ug. Can use TB syringe to dose.
- b. Duration 8 - 24 hours.
- c. Redosed when polyuria returns.
- d. Most commonly used treatment today.
- e. Use the intranasal preparation.

2. Chlorpropamide (Diabenese)

- a. Oral hypoglycemic. Stimulates ADH release and potentiates ADH action. Hypoglycemia is the limiting factor.
- b. 25 - 40 mg once or twice a day (cat). Limited experience.

C. Treatment of NDI

1. Salt restriction

2. Thiazide diuretics:

- a. Natriuresis results in a decrease in blood volume and increased sodium reabsorption in the proximal tubule.
- b. Hydrochlorothiazide 12.5 - 25 mg once or twice a day (cat).
- c. Chlorthiazide 20 - 40 mg/kg BID (dogs).
- d. May also help with partial CDI.

D. Treatment of Primary Polydipsia

1. Treatment to restore hypertonic renal medullary interstitium.
2. Gradual water restriction over several days.
3. Behavioral modification or referral to a behaviorist may be needed.